PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 3024-119

I hereby certify that this pre-appeal brief request form is filed via the USPTO's EFS

on 2/9/12

Signature /Joyce v. Natzmer/

Typed or printed name Joyce von Natzmer

Application Number	Filed
10/595,495	April 24, 2006

First Named Inventor: Mermod

Art Unit	Examiner
1636	Celine X. Qian

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 48120.
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

/Joyce v. Natzmer/
Signature

Joyce von Natzmer
Typed or printed name

301-657-1282
Telephone number

2/9/12
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
Mermod et al.	)	Atty. Dkt. **3024-119**
	)	
Appl. No. **10/595,495**	)	
	)	Examiner: Celine X. Qian
	)	
371(c) date: 04/24/06	)	Group Art Unit: 1636

For: **HIGH EFFICIENCY GENE TRANSFER AND EXPRESSION IN MAMMALIAN CELLS BY A MULTIPLE TRANSFECTION PROCEDURE OF MAR SEQUENCES**

REMARKS ACCOMPANYING PRE-APPEAL CONFERENCE REQUEST

Mail Stop: AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the final Office Action of September 9, 2011 and following applicants' After Final Amendment of November 9, 2011 and the Office's Advisory Action of November 18, 2011, applicants submit the following remarks accompanying applicant's request for a pre-appeal conference and notice of appeal.

Remarks begin on page 2 of this paper.

REMARKS

Apart from a readily addressable antecedent basis issue in claim 125, the rejection remaining in this case, is the written description rejection, which begins on page 2 of the Office Action of September 9, 2011. Here, the Office continued to reject claims 65, 67, 68, 70-72, 74-91, 103, 105-107, 111-115, 117-119 and 122-126 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The Office noted that applicants had amended independent claim 65 to require a genus of nucleic acid sequences having >=90% homology with SEQ ID NO: 25. The Office stated that since SEQ ID NO: 25 consists 3616 base pair nucleotides, a sequence having 90% homology may contain at least 361 mutations within any position of the nucleotide sequence.

The Office also took the position that the specification does not disclose whether any sequence with 33% TA and/or 33% AT on a stretch of 100 base pairs and any type of DNA binding site would have protein producing increasing activity in any setting. The Office further took the position that the specification does not describe any nucleotide sequences having 90% homology with SEQ ID NO: 25 that still possesses MAR activity. Finally, the Office took the position that the specification also fails to teach specific regions within SEQ ID NO: 25 that are responsible for the claimed MAR function (*emphasis added*).

Claim 65 reads:

> "A purified and isolated DNA sequence comprising:
> a) at least one bent DNA element comprising at least 33% of the dinucleotide TA and/or at least 33% of the dinucleotide AT on a stretch of 100 contiguous base pairs,
> b) at least one binding site for a DNA binding protein,
> wherein said purified and isolated DNA sequence is
> a MAR nucleotide sequence with sequence ID NO: 25, or
> a sequence complementary to sequence ID NO: 25, or
> a sequence having at least 90% identity with said SEQ ID NO: 25." (*emphasis added*)

As can be seen from the above, claim 65 refers to a MAR nucleotide sequence. Claim 65 does not refer to a protein producing increasing activity, a MAR activity or a MAR function. The specification refers to a protein producing increasing activity, a MAR activity and a MAR functional activity.

"MARs" are described, e.g., in paragraph [0064] of the publication of the present application (US Pub. **20070178469**). Here the specification states:

> "MARs", according to a well-accepted model, may mediate the anchorage of specific DNA sequence to the nuclear matrix, generating chromatin loop domains that extend outwards from the heterochromatin cores. While MARs do not contain any obvious consensus or recognizable sequence, their most consistent feature appears to be an overall high A/T content, and C bases predominating on one strand (Bode J, Schlake T, RiosRamirez M, Mielke C, Stengart M, Kay V and KlehrWirth D, "Scaffold/matrix-attached regions: structural propreties creating transcriptionally active loci", Structural and Functional Organization of the Nuclear Matrix: International Review of Citology, 162A:389453, 1995). These regions have a propensity to form bent secondary structures that may be prone to strand separation. They are often referred to as base-unpairing regions (BURs), and they contain a core-unwinding element (CUE) that might represent the nucleation point of strand separation (Benham C and al., Stress induced duplex DNA destabilization in scaffold/matrix attachment regions, J. MoL BioL, 274:181-196, 1997). Several simple AT-rich sequence motifs have often been found within MAR sequences, but for the most part, their functional importance and potential mode of action remain unclear. These include the A-box (AATAAAYAAA), the T-box (TTWTWTTWTT), DNA unwinding motifs (AATATATT, AATATT), SATB1 binding sites (H-box, A/T/C25) and consensus Topoisomerase II sites for vertebrates (RNYNNCNNGYNGKTNYNY) or Drosophila (GTNWAYATTNATNNR)." (*emphasis added*)

In view of the lack of functional language in the present claims, applicants submit that claim 1 of Example 11A of the written description training material (March 25, 2008, hereinafter "WDTM") is directly applicable to the sequence identity issue. Claim 1 of Example 11A refers to:

> "An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2."

The training material provides the following analysis of the claim:

> "Claim 1 encompasses nucleic acids that encode the polypeptide of SEQ ID NO: 2, as well as those that encode any polypeptide having 85% structural identity to SEQ ID NO: 2. However, the specification discloses only a single species that encodes SEQ ID NO: 2; *i.e.,* SEQ ID NO: 1.
> There are no other drawings or structural formulas disclosed that encode either SEQ ID NO: 2 or a sequence with 85% identity to SEQ ID NO: 2.
>
> The recitation of a polypeptide with at least 85% identity represents a partial structure, that is, at least 85% percent of the amino acids in the polypeptide will match those in SEQ ID NO: 2, and up to 15% of them may vary from those in SEQ ID NO: 2. However, there is no teaching regarding which 15% of the amino acids may vary from SEQ ID NO: 2. Consequently, there is also no information given about which nucleotides will vary from SEQ ID NO: 1 in the claimed genus of nucleic acids. There is no functional limitation on the nucleic acids of claim 1 other than that they encode the polypeptide of SEQ ID NO: 2 or any polypeptide having 85% structural identity to SEQ ID NO: 2. The genetic code and its redundancies were known in the art before the application was filed.
> The disclosure of SEQ ID NO: 2 combined with the pre-existing knowledge in the art regarding the genetic code and its redundancies would have put one in possession of the genus of nucleic acids that encode SEQ ID NO: 2. With the aid of a computer, one of skill in the art could have identified all of the nucleic acids that encode a polypeptide with at least 85% sequence identity with SEQ ID NO: 2. Thus, one of ordinary skill in the art

would conclude that the applicant was in possession of the claimed genus at the time the application was filed.

Conclusion:
The specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the scope of claim 1."

The WDTM do not refer to the length of SEQ ID NO:1 and/or 2. See also Example 10, claim 2 of the WDTM.

In this context, applicants would like to refer the Office also to claims 105, 106, 107, 119 and 124 which further define sequence identities, partially combined with further structural features. Furthermore claim 117 only refers to sequences complementary to SEQ ID NO: 25. All of these claims are part of the written description rejection. Applicants submit that the Office has issued a written description rejection based on limitations that are not present in the all claims rejected (compare, e.g., claim 12). Applicants submit that this claims interpretation appears, among others, not to be consistent with MPEP 2111, which states that during patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification."

Reconsideration of the rejection is therefore respectfully requested.

No fees in addition to the fees submitted herewith are believed to be due. However, the Commissioner is authorized to charge undersign's deposit account 50-3135 for any additional fees or overpayments. Any extension(s) of time that may be required is/are respectfully requested herewith.

Respectfully submitted,

By: /Joyce v. Natzmer/
Joyce von Natzmer
Registration No. 48,120
Customer No. 46002
Telephone: (301) 657-1282

Pequignot + Myers, LLC
200 Madison Ave., Suite 1901
New York, NY 10016

February 9, 2012